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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/091,578	10/06/98	MADISON	E 19191.0002

HM22/0504

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EXAMINER	
DIBRINO, M	
ART UNIT	**PAPER NUMBER**
1644	18

DATE MAILED: 05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/091,578	Madison et al
Examiner	**Art Unit**
Marlann DiBrino	1644

-- The MAILING DATE of this communication appears on th cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 21, 2001*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *3 and 13-66* is/are pending in the applica

4a) Of the above, claim(s) *25-64* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *3, 13-24, 65, and 66* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☒ Interview Summary (PTO-413) Paper No(s). 16

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Applicant's amendment filed 2/21/01 is acknowledged and has been entered.

Claims 3, 13-24, 65 and 66 are presently being examined.

The following are new grounds of rejection necessitated by the amendment filed 2/21/01.

2. Applicant is reminded of the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999; the following rejection is set forth herein.

3. Claims 3, 13-24, 65 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed: (1) protein consisting of a grafted optimized protein surface loop that specifically binds a selected target, wherein the protein surface loop is not endogenous to the protein and replaces a surface loop on the protein; (2) wherein the target is a biological entity, a synthetic or naturally occurring macromolecule, a protein or an "IgG-like" molecule.

The instant claims encompass a protein *consisting of* a protein surface loop that is not endogenous to the said protein and replaces a surface loop on the protein (i.e., the protein *consists of* the protein surface loop), and wherein the target is biological entity, including an organism or a human, a synthetic or naturally occurring macromolecule, including synthetic macromolecules not found in nature or in a living organism, as well as any naturally occurring organic or inorganic macromolecule. There is insufficient disclosure in the specification on such a protein and such targets.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d

1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of an antigen "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description ... requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; Id. at 1170, 25 USPQ2d at 1606.

The specification discloses (on page 12 at lines 19-29) that a surface loop is defined as a binding, i.e., targeting, element of a protein which element is a flexible loop structure in the native protein of about 2 to about 20 amino acids that either connects regions of defined secondary structure in the native protein or connects a domain of secondary structure and a terminus of the native protein, and which element is selective for binding to one or more binding sites. The specification further discloses a list of "targets" on page 13 at lines 23-31 and continuing onto page 14 at lines 1-6. "Targets" include, but are not limited to, for example, any region, tissue, organ, cell, virus, organelle, microorganism, synthetic or naturally occurring molecule or macromolecule, a modified variant thereof, a protein, a receptor, a proteoglycan, an ion channel, a biological entity, or a component of a pathologic lesion. The specification (on page 34) also discloses tPA protein comprising an optimized surface loop from Fab-9 mAb which binds β3-integrins.

The instant disclosure does not adequately describe the scope of the claimed invention, which encompasses a substantial variety of subgenera. Since the disclosure fails to provide sufficient relevant identifying characteristics that identify members of the genus, and given the broad genus claimed, the disclosure of the tPA/Fab-9 surface loop protein is insufficient to describe the claimed genus. There are insufficient relevant identifying structural characteristics disclosed by the instant specification for the claimed proteins/targets.

4. Claims 3, 13-24, 65 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the specification and claims as originally filed is: "wherein the protein is not an antibody" (recited in instant claim 3).

5. Claims 3, 13-24, 65 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to make and/or use a protein *consisting of* a grafted protein surface loop that specifically binds a selected target, wherein the protein surface loop is not endogenous to the protein, replaces a surface loop on the protein. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a protein that is a peptide.

The specification discloses (on page 12 at lines 19-29) that a surface loop is defined as a binding, i.e., targeting, element of a protein which element is a flexible loop structure in the native protein of about 2 to about 20 amino acids that either connects regions of defined secondary structure in the native protein or connects a domain of secondary structure and a terminus of the native protein, and which element is selective for binding to one or more binding sites. The specification further discloses a list of "targets" on page 13 at lines 23-31 and continuing onto page 14 at lines 1-6. "Targets" include, but are not limited to, for example, any region, tissue, organ, cell, virus, organelle, microorganism, synthetic or naturally occurring molecule or macromolecule, a modified variant thereof, a protein, a receptor, a proteoglycan, an ion channel, a biological entity, or a component of a pathologic lesion. The specification (on page 34) also discloses tPA protein comprising an optimized surface loop from Fab-9 mAb which binds β3-integrins.

Evidentiary reference Dorland's Illustrated Medical Dictionary (27th Ed., 1988) defines proteins as being of high molecular weight and consisting of amino acid residues (page 1370). Dorland's defines peptide as being a low molecular weight compound made of amino acid residues (page 1254).

There is insufficient guidance in the specification as to how to make and/or use the instant invention. There is no disclosure in the specification as to making/using a protein *consisting of* a grafted optimized protein surface loop. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 13, 19, 22, 24 and 65 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 24 recites the limitation "targeted agent" in line 1. There is insufficient antecedent basis for this limitation in the claim because base claim 23 does not recite the said limitation.

b. Claim 19 is indefinite in the recitation of " Arg-Gly-Asp (RGD) tripeptide motif" because it is ambiguous to recite a limitation within parentheses.

c. Claim 24 is indefinite in the recitation of "(CDR3)" because it is ambiguous to recite a limitation within parentheses.

d. Claim 65 is indefinite in the recitation of ""(LG-tPA)"because it is ambiguous to recite a limitation within parentheses.

e. Claim 13 is indefinite in the recitation of "biological entity" because it is not clear what is meant.

f. Claim 22 is indefinite in the recitation of "IgG-like molecule" because it is not clear what properties of the IgG molecule are intended to be within the metes and bounds of the claimed invention.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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